REMARKS

The Office Action of March 26, 2009 was received and carefully reviewed. Claims 3, 4 and 7 were pending prior to the instant amendment. Claim 7 is canceled. Claims 8-10 are added. Consequently, claims 3-4 and 8-10 are currently pending in the instant application. Reconsideration and withdrawal of the currently pending rejections are requested for the reasons advanced in detail below.

No rejection(s) have been made against claims 3 and 4. Presumably, claims 3 and 4 are believed to be in condition for allowance. Accordingly, an indication of allowance is respectfully requested from the Examiner.

Claim 7 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Nomura et al. (U.S. Patent No. 6,387,908 B1, hereinafter "Nomura") and their application 09/508026 filed May 5, 2000, and in further view of Stahl et al. (Handbook of Pharmaceutical Salts, Properties, Selection, and Use., Verlag Helvetica Chimica Acta, Zurch, 2002, hereinafter "Stahl"). Without conceding the propriety of the rejection, claim 7 has been canceled.

New claim 8 is submitted herewith as an amended version of previous claim 1. Claim 8 recites a specific combination of features that distinguishes the invention from the prior art in different ways. For example, independent claim 8 recites a combination that includes, among other things:

> *". . . DSC measured at a heating elevation rate of 2°C/minute: exothermic peak observed at a temperature in the range of 170 to 175°C with weight decrease."*

Support for the amendment is found, at least, in Applicant's originally filed specification on page 22, lines 25-26 (heating elevation rate of 2°C/minute). The definition of the heating elevation

rate is intended to clarify the conditions for the determination of DSC curve.

Applicant wishes to note that the IR data, as originally recited in previous claim 1, has been deleted from newly submitted claim 8. It has now been confirmed that there is no significant difference on the IR spectrum between the mainly amorphous product obtainable by Nomura (Example 48) and the crystalline product of the present invention (Example 9 of the present specification). When the subject application was filed, the inventors understood that there was a difference in the IR spectrum between the product of Nomura and that of the present invention. The response to the first Office Action (filed on March 27, 2008) to point out the difference of the IR spectrum was prepared on this understanding. As is explained in the attached Declaration, the inventors have recently noted that the difference in the IR spectrum was caused by differences in the instrument or experimental conditions.

One of the inventors – Mr. Toshihiro Takahashi – has newly obtained the IR spectrum of the product of Nomura and that of the present invention using the same instrument under the same experimental conditions. The results of the new experiments have proven that there is no significant difference in the IR spectrum measured the on KBr tablet. The results are set forth in the enclosed Declaration pursuant to Rule 132 (and the attached FIGS. 1-5). Thus, for the reasons mentioned above, the IR data has been excluded from newly submitted claim 8 (amended version of previous claim 1). Further, Applicant now cancels or withdraws the discussions related to the IR spectrum as discussed in the response (filed on March 27, 2008) to the first Office Action (e.g., see the last paragraph of page 6 and the third paragraph of page 7).

Applicant further submits additional arguments, regarding new claim 8, in view of previous claim 1. First, Applicant notes that Example 48 of Nomura (see column 23, lines 35-

49) corresponds to the Na salt given in Table 1 of Applicant's specification on page 23, lines 8-9 (obtained according to the conventional process). Second, Applicant further notes that Example 9 (discussed in the specification on page 18) corresponds to the Na salt listed in Table 1 of Applicant's specification on page 23, lines 14-15 (obtained in Example 9). The salt of Example 9 is included in claim 8.

Clear distinctions exist between the mainly amorphous product obtainable in Example 48 of Nomura and the crystalline product of the present invention. Nomura discloses sodium (2S,3S)-3-[[(1S)-1-isobutoxymethyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylate in Example 48 (column 23, lines 35-49). Nomura does not describe characteristics of the product of Example 48 except for IR data and ^{1}H NMR data. The compound disclosed in Nomura is a mainly amorphous product (as is shown in the specification of the subject application in Table 1 (see page 23, on lines 8-9 (amor.>crys)) and further evidenced from the data given in the attached Declaration), while claim 8 of the present invention defines a crystalline product.

In accordance with the Declaration, submitted herewith, Mr. Takahashi (one of the inventors) submits previously obtained data and new data obtained by newly conducted experiments. The additional comparative experiments further clarify the difference between the disclosure of Nomura and the present invention. The data and the results are shown in the attached Declaration.

Sample 1 was prepared in the same manner as in Example 48 of Nomura at column 23, lines 35-49. Sample 2, according to the present invention, was prepared in the same manner as in Example 9 (see the present specification on page 18). The microscopic pictures and powder X-ray diffraction data (PXRD) of Samples 1 and 2 were compared. As is evident from

the photographs and charts shown in FIGS. 6-17, the mainly amorphous product, obtained in Example 48 of Nomura, is distinctly different from the crystalline product of the present invention.

In addition, the mainly amorphous product obtainable in Example 48 of Nomura is outside the scope of the present invention from the viewpoint of DSC peaks defined in claim 8 (i.e., 170 to 175°C). For the sake of confirmation, Samples 1 and 2 were analyzed using DSC at a heating elevation rate of 2°C/minute or 5°C/minute in a manner similar to Example 15 (given in Applicant's specification on page 22). It is observed that the differences in the heating elevation rates affect exothermic peak temperatures of the crystalline product of the present invention in the DSC, as is shown in Table III of the Declaration. Notably, claim 8 defines the heating elevation rate at 2°C/minute.

In the final Office Action (mailed September 15, 2008), the Examiner alleges that the minor differences in the presented DSC data of Table 1 of the instant disclosure could easily be attributed to solvent content in view of the various drying techniques cited (see page 2, lines 15-17). Accordingly, experiments have been conducted to confirm whether the differences in the DSC data can be attributed to solvent content in view of the drying conditions. The results are included in the attached Declaration. The results in Table II of the Declaration show that the differences in the DSC data cannot be attributed to solvent content.

The Examiner further alleges that there is no evidence that the IR or DSC data of the amorphous material of instant salts (E), or the Nomura salts of compound 87, vary to any significant extent from that reported for the instantly recrystallized salts (E) (see page 2, lines 13-15 of final Office Action). However, the salts (E) described in the present specification are not

disclosed in Nomura. Accordingly, the salts (E) do not embody the product of Nomura. Further, the salts (E) do not embody the product of the present invention. The crystalline product of the present invention corresponds to the immediately dried Na crystalline products (G) described in Example 9 of the present specification (on page 18). Hence, the discussion of salts (E), is not applicable to the prior art or to the present invention.

The crystalline product, as recited in claim 8, is clearly different from the product of Nomura. The claimed product shows an improved stability (95-98% remains after 3 days at 80°C), as is shown in Table 1 of the present specification (e.g., see page 23, line 14). The effect of the present invention cannot be expected from the disclosure of Nomura, as is shown in Table 1 of the present specification on page 23, line 8 (13-77% remains after 3 days at 80°C). Accordingly, Applicants submit that the present invention, as claimed, would not be anticipated by Nomura, since each and every element, as set forth in the claims are not found either expressly or inherently described as required by the M.P.E.P. Furthermore, Stahl fails to disclose or fairly suggest the missing elements of Nomura. Hence, Nomura, in view of Stahl, fails to establish a *prima facie* case of obviousness of the claimed invention, since all the claim limitations are not taught or suggested by the prior art in accordance with the M.P.E.P. § 2143.03

New claim 9 is submitted herewith. Support for the claim is found, at least, in Applicant's specification on page 23, line 14 (crystalline needles) in Table 1. Claim 9 depends from independent claim 8 and is patentable over the cited prior art for at least the same reasons as set forth above with respect to claim 8.

New claim 10 is submitted herewith and further defines the IR data. Claim 10 depends from independent claim 8 and is patentable over the cited prior art for at least the same reasons

as set forth above with respect to claim 8.

In addition, each of the dependent claims also recites combinations that are separately patentable.

In view of the foregoing remarks, this claimed invention is not rendered obvious in view of the prior art references cited against this application. Applicant therefore requests the entry of this response, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

In discussing the specification, claims, and drawings in this response, it is to be understood that Applicant in no way intends to limit the scope of the claims to any exemplary embodiments described in the specification and/or shown in the drawings. Rather, Applicant is entitled to have the claims interpreted broadly, to the maximum extent permitted by statute, regulation, and applicable case law.

Should the Examiner believe that a telephone conference would expedite issuance of the application, the Examiner is respectfully invited to telephone the undersigned patent agent at (202) 585-8316.

Respectfully submitted,

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